AMERICAN JOURNAL OF PHARMACY

and

THE SCIENCES SUPPORTING PUBLIC HEALTH

SINCE
1825

HENRY V. ARNY
1868—1943

DECEMBER
1943

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Since 1825

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IN MEMORIAM

HENRY V. ARNY

1868-1943

FEW pharmacists in America have not heard the name of Arny associated with some important phase of pharmaceutical endeavor. The death of Dr. Henry V. Arny on November 3, 1943 brings a feeling of loss as another of pharmacy's outstanding and unforgettable characters passes on.

Dr. Arny was born in Philadelphia in 1868 but he received his elementary education in New Orleans, La. He returned to Philadelphia for his pharmaceutical education, graduating with distinction from the Philadelphia College of Pharmacy in 1889. After working in New Orleans for three years he studied in the University of Berlin and the University of Göttingen where in 1896 he received his Ph. D. degree "magna cum laude." In 1897 he became professor of pharmacy at the Cleveland School of Pharmacy (Western Reserve) and later became Dean. In 1911 Dr. Arny assumed the chair of pharmaceutical chemistry at the New York College of Pharmacy (Columbia University) and was its Dean from 1930 until his retirement in 1937.

During his lifetime Dr. Arny's contributions were most numerous. He was author of the well-known text book "Principles of Pharmacy" and was on the editorial staff of a number of pharmaceutical journals. In 1922 he received the Remington Medal for outstanding service to pharmacy and the Ebert Medal in 1926. Dr. Arny was past president of both the American Pharmaceutical Association and the American Conference of Pharmaceutical Faculties. He rendered invaluable service on both the Revision Committee of the United States Pharmacopœia and the National Formulary Committee.

In the words of one of his contemporaries who knew him well, "Dr. Arny was a most distinguished gentleman, a man of the finest personality, ideals and scientific accomplishments. He gave liberally and unselfishly in worthwhile service to pharmacy and his fellowman." No finer tribute could be given any man!

EDITORIAL

THE KILGORE BILL

ELSEWHERE in this issue is an article by one of our frequent contributors which decries the opposition which has arisen in scientific and professional circles to the Kilgore Bill. Only our firm belief in freedom of the press and individual expression has led us to print this article. We are quite sure that most of our readers will disagree with Mr. Harding most vehemently.

The Kilgore Bill (S. 702) is another of those pieces of legislation not unlike the Wagner, Murray, Dingell bill in its implications, namely, that the government should regulate and control each and every act of our daily lives in order that we may be protected from all the evils of private enterprise so that much greater progress and happiness may be had by all.

We have in many high places in our government a number of men who do not believe in our concept of the American way of life. They are trying by every means known to them to change our economic and social system into one in which each citizen becomes a pawn of bureaucratic control. We shall be told what to eat, where to go, to how much education we can aspire, for what work we are best fitted, when to retire and on what pension, and so on *ad infinitum.* We would become children of the state and our own likes and dislikes, aims and objectives would perforce be subjugated to what some government administrator thought was best—an ideal life no doubt!

The many restrictions that have been placed on us by the present war cannot be helped and all loyal Americans endure them tolerantly, but we must not allow our love of freedom to be so dulled that we permit ourselves to be saddled with regimentation *permanently* lest we forget what freedom means. This is exactly what frequently happens when a man, after being imprisoned for years, is suddenly released—he often has forgotten how to live and longs for the protection of prison walls!

Those that support regimentation are a motley crowd. Generally we have first those who are in public office usually by appointment rather than election, and the sense of power that they have over mere John Does is like heady wine—one taste demands more. Then we

have some few children of the rich who, having led an irresponsible life, seek amends by professing a belief in socialism, communism or other ism which attitude can best be explained by the psychologists. Lastly and most important we have labor. Led by leaders who have affiliations with government, labor endorses all legislation tending to government control not realizing that when complete control comes, the right to strike, collective bargaining *et al.* is gone. Can those in Civil Service, the Army or Navy strike against proper authority?

The only strong force in America which can speak against regimentation are the scientists to whom freedom is both a cherished possession and a holy trust. Down through the centuries it has been their task to seek for truth and to resist all efforts to suppress it. In those countries where despotism has flourished it has often been men in academic circles, scientists, the clergy or others who broke the bounds and set men free. In all fascist countries today the rigid control of all universities is one of the requirements for continued tyranny.

We are not against planned research, in fact we believe that research is well planned in this country else we would not be the world's most progressive nation and the envy of all others. We do object to bureaucratic control and having research dictated and directed by politicians. In a like manner we believe in group medicine as long as free enterprise and the freedom to select one's doctor or hospital continues. Those in government service cannot be expected to understand our views since we do not want their meddling or supervision. It is up to us to insist that since they are our chosen representatives and in reality public servants they must represent our views and not dictate our future. This is still, in part at least, a government operated in accordance with the wishes of the electorate and not in conformity with professional reformers and those who would completely revamp our way of life.

Our very real danger is that these golden plans and promises may so appeal to the masses that they are passed over our objections. If this happens then freedom for all will vanish and it may never again be man's lot to exercise his God-given privilege of freedom and creative expression.

L. F. Tice

A HISTOLOGICAL COMPARISON OF THE RHIZOMES AND STIPES OF DRYOPTERIS FILIX-MAS WITH THOSE OF CERTAIN OTHER MEMBERS OF THE POLYPODIACEAE FAMILY †

By Albert H. Musick * and Heber W. Youngken, Jr., Ph. D.**

ASPIDIUM, U. S. P. XII, consists of the rhizome and stipes of *Dryopteris Filix-mas* (L) Schott, known in commerce as European Aspidium or Male Fern, or of *Dryopteris marginalis* (L) Asa Gray, known in commerce as American Aspidium or Marginal Fern (Fam. Polypodiaceæ) (1). According to Youngken (2), Gathercoal (3), Trease (4), and Tschirch (5), the rhizomes of other ferns such as those of *Osmunda claytonia* L., *Athylrium Filix-fœmina* L., and *Aspidium spinulosum* Sw. have been frequently substituted for those of the official drug. The macroscopical and histological description of these adulterants have been described in detail in the literature (6), (7), (8), (9).

Other members of the Polypodiaceæ family occurring in the Pacific Northwest and considered as possible substitutes are: *Dryopteris arguta* (Kaulfuss) Watson, *Dryopteris oregana* C. Christensen, *Polystichum andersoni* Hopkins, *Woodwardia radicans* (L) Swartz, *Athyrium alpestre* var. *americanum* Butters, *Asplenium trichomanes* L., and *Cryptogramma acrostichoides* R. Brown.

This study has then the purpose of establishing type descriptions for the rhizomes and stipes of the above ferns so that their presence in commerce may be confirmed more satisfactorily.

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† An abstract of a thesis presented to the faculty of the University of Washington in partial fulfillment of the requirement for the degree of Doctor of Philosophy, June, 1943.

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** Instructor in Pharmacognosy, College of Pharmacy, University of Washington, Seattle, Washington.

Investigation

Methods and Materials—The fern plants selected for this study were obtained by the author in the vicinity of Seattle, Washington, and verified by members of the herbarium staff of the Department of Botany and by members of the Department of Pharmacognosy, University of Washington. The various fern rhizomes and stipes were killed and fixed with formalin-aceto-alcohol, dehydrated by the butyl alcohol method, imbedded in paraffin (10), transverse and longitudinal sections cut on the rotary microtome, differentially stained with fast green and safranin and permanent mounts prepared. Many free hand sections were prepared and examined to supplement the permanent mounts. In the making of free hand sections the following standard stains and reagents (11) were used: phloroglucin-HCl solution and saturated aqueous solution of aniline sulfate (for cell lignification); concentrated sulfuric acid (for suberose walls); aqueous solution of chlorzinc-iodide (for cellulose walls); aqueous solution of chloral hydrate (for clearing); iodine water and/or iodine-potassium iodide solution (for starch); and, aqueous solution of copper acetate (for tannin). Representative photomicrographs and illustrations were included with each description.[1]

Descriptions of the 2 official ferns were carefully rechecked and used in the study as standards for a comparison.

I. *Dryopteris Filix-mas* (L) Schott.

Macroscopic—The rhizomes are woody and stout, occurring either erect or decumbent in the soil. In shape they are cylindrical and nearly straight, or curved and tapering toward one end. They range in thickness from 1 to 3 cm. Feathery masses of pale yellow to reddish-brown membranous scales or ramenta, linear to lanceolate in outline adhere to the rhizome and stipes. Internally the rhizome is green in color.

Histology of the Rhizome: Epidermis—The epidermis of *D. Filix-mas* consists of a single layer of cells varying in size from roundish to oblong and closely associated together. These cells are brownish in color and contain occasional tannin-resin masses. Many

[1] The thesis contains 29 photomicrographs and 23 illustrations of the external structures.

of the cells give off ramenta or scales composed of elongated thin-walled cells, with the marginal cells prolonged at intervals into simple hair-like processes or projections, each projection consisting of 2 parallel and contiguous cells. No glands are present on the scales, except at the base where there are sometimes two (Fig. 1).

Outer Cortex—Beneath the epidermis there is formed an accessory protective layer of partially lignified, thick-walled cells, reinforcing the epidermis, and called the hypodermis. These cells are orange to brownish-yellow in color and vary in shape from ovate to oblong-elliptical in cross section. In longitudinal section these cells are elongate, usually with pointed ends, and possess a few round pits. The hypodermis consists usually of 3 to 8 layers of cells.

Inner Cortex—This tissue consists of many layers of large, isodiametric and polygonal cells, parenchymatous in nature, and with thin cellulose walls. The cell walls are variable in thickness, frequently colorless, but may show varying tints of yellow or brown. Faint glimpses of the plasmodesma may be seen in the thick-walled cells. These are long, of comparatively large diameter and lie in minute passages which in most cells constitute the only break in the continuity of the wall. In longitudinal section they are predominantly rectangular in shape.

The starch grains are numerous in the cortical region and vary in length from 2 to 23 microns with an indistinct hilum and lamellæ. They vary in shape from elliptical, ovoid, and oblong to irregular with the irregular and elliptical grains predominating.

Tannin was found to be quite abundant in the cortical parenchyma. Sections of the rhizome were mounted in 7 per cent aqueous solution of copper acetate and examined under the microscope. A marked color change in cell contents took place almost immediately, an insoluble brownish precipitate being produced in those cells containing tannin. Occasional brownish-orange masses of resinous material were encountered.

Numerous large intercellular air spaces occur, many of which contain short-stalked, pear-shaped internal glandular hairs with greenish-yellow contents. The glandular heads measured up to 35 microns in diameter.

Pith—The pith is a roughly cylindrical body of tissue in the center of the rhizome and is continuous with the cortex. It is made up of rather uniform parenchymatous tissue in which the cells are arranged somewhat loosely with many intercellular spaces. Many of these intercellular spaces contain short-stalked, pear-shaped internal glandular hairs with greenish-yellow contents. The glandular heads also measure up to 35 microns in diameter. In shape, the cells of the pith are mostly rounded, isodiametric, polygonal, or cylindrical with thin cellulose walls and are filled with starch. Tannin is also present.

Arrangement of the Vascular Bundles—The mature stem portions are polycyclic [2] and possess several more or less diffuse concentric cylinders of vascular tissue. The arrangement of the vascular bundles is dictyostelic, the individual bundles being known as meristeles. The meristeles are protostelic in construction, i. e., the phlœm surrounds the xylem in a rod-like column. This type of bundle is also called xylocentric, or concentric and amphicribral in arrangement. The meristeles are elliptical, oval, or oblong in shape. In cross section the stem bundles are 8 to 10 in number and are arranged in a diffuse circle imbedded in the parenchyma. The leaf trace bundles are smaller, similar in shape to the stem bundles, and are scattered externally alongside the stem bundles. Each vascular bundle is surrounded by a single layer of endodermal cells. In longitudinal section these smaller leaf trace bundles may be seen to come off the stem bundles and pass out through the cortex into the leaves.

Description of the Component Parts of the Bundle: Endodermis—The endodermis of *D. Filix-mas* is a cylindrical sheet of cells, 1 layer thick, without intercellular spaces and completely enveloping the bundle. In cross section the individual cells appear rectangular in shape while the cell walls are brownish-yellow and the cell contents a granular, greenish-yellow. In longitudinal section the side of the cell toward the cortex is thin-walled, while the side of the cell toward the pericycle is thick-walled. The end walls appear to be thickened and blunt or square. An extremely narrow and thread-like strip runs completely around the cell on the inner surface of the radial

[2] Many references to details of stellar structure appear in the body of the thesis, but are too numerous to include in this paper. An excellent summary appears in Smith (12).

and end walls and is cutinized or suberized. These are the Casparian strips. Starch and tannin are absent in this cell layer.

Pericycle—The pericycle is a thin cylinder of tissue sheathing the vascular tissues, limited internally by the primary phloem and externally by the endodermis. In cross section the cells appear polygonal, oblong, or rectangular in shape. The pericycle varies in width from 1 to 3 rows of thin-walled, non-lignified parenchymatous cells filled with protoplasm. Starch granules and amorphous tannin deposits may be seen in this region.

Phloem—The phloem consists of sieve tubes and phloem parenchyma. In cross section the sieve tubes are polygonal in shape. In longitudinal section they appear as elongated, spindle-shaped, pointed cells with watery contents and thin cellulose walls. The cells are arranged more or less definitely in longitudinal rows and form a series by the connection of their protoplasts through small openings in the wall. These perforations occur in groups in restricted thin areas called sieve plates. According to Eames and MacDaniels (13) the limits of the sieve tubes in the pteridophytes are not as well defined as in the angiosperms where they are sharply set off from the thicker part of the wall. The sieve plate is divided into sieve fields by a network of thicker strips, though these are not sharply defined. Through each sieve field pass several to many plasmodesma-like strands which extend between highly refractive globules that adhere to the walls. Eames and MacDaniels (14) state that in the pteridophytes the phloem contains only sieve tubes and phloem parenchyma. Phloem parenchyma occurs interspersed among the sieve tubes.

Xylem—The chief features of the xylem are the tracheids which are large and have a very characteristic polygonal outline. The cell walls are lignified as shown by phlorglucin-HCl solution or by an aqueous solution of aniline sulfate and are without protoplasts. In longitudinal section the tracheids are elongate, spindle-shaped cells with thickened lignified walls marked by bordered pits. The pits are transversely elongated and lie parallel to one another. They are known as scalariform tracheids from the ladder-like appearance. These larger tracheids constitute the metaxylem or that portion of the xylem that has matured after elongation of the cell has ceased.

The protoxylem, or first matured portion of the xylem, lies usually at both ends of the ellipse of xylem. It is distinguished from the metaxylem by its small size in cross section and from a study of the longitudinal sections which show annular and spiral rings. The first tracheids that mature in the xylem have the additional wall material deposited in transverse rings, thus the derivation of the term annular. If the material is deposited in a continuous spiral, a spiral tracheid is formed. Centripetal xylem is formed, the xylem group or strand then being called exarch, because the development of the xylem is toward the center or axis of the plant. In exarch xylem the metaxylem lies internal to the protoxylem. Xylem parenchyma occurs interspersed among the tracheids.

Histology of the Stipe—The histology of the stipe of *D. Filix-mas* is essentially the same as that of the rhizome except that the hypodermis appears completely lignified and the inner cortex is devoid of leaf-trace bundles.

II. *Dryopteris marginalis* (L) Asa Gray.

Histology of the Rhizome and Stipe—After personal observation and a communication from Dr. Heber W. Youngken[3] (15) it was established that there were no important differences except measurements of a microscopical character between the histology of the rhizomes and stipes of *D. Filix-mas* and *D. marginalis*. Based upon the examination of sections taken at different levels from the summit to the base of the stipe, Finklestein (16) has reported a range of from two to thirteen xylocentric bundles.

III. *Dryopteris arguta* (Kaulfuss) Watson.

Macroscopic—The rhizomes are woody and stout, occurring either erect or decumbent in the soil. They are cylindrical and nearly straight in shape, or curved and tapering toward one end. They range in thickness from 1 to 3 cm. Numerous, bright, chestnut brown, thin, oblong to lanceolate, attenuate scales adhere to the rhizomes and stipes. The rhizome is green in color internally as in the official Aspidiums.

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[3] Specimens of *D. marginalis* were obtained from and authenticated by Dr. Heber Youngken, Professor of Pharmacognosy and Biology in the Massachusetts College of Pharmacy, Boston, Mass.

Microscopic—D. arguta differs from the official Aspidiums as follows: Many of the epidermal cells give off scales composed of elongated, thin-walled cells, with the marginal cells prolonged at intervals into simple, hair-like processes or projections, each projection consisting of two parallel and contiguous cells. Small, round, short-stalked glands are found on the margins of the scales, the glandular heads measuring up to 60 microns in diameter. Similar glands may be found upon the epidermis (Fig. 2). The stem bundles are eight to ten in number. In the stipe the cell wall between the endodermis and the inner cortex is excessively thickened, or about 9 to 10 microns in thickness. Three to seven xylocentric vascular bundles are imbedded in the parenchyma forming the central matrix of the stipe.

IV. *Dryopteris oregana* C. Christensen.

Macroscopic—The rhizomes are slender and creeping, the apical portions being covered with the imbricate stipe bases of old fronds. These rhizomes usually occur decumbent in the soil. They are cylindrical and nearly straight in shape, or curved and tapering toward one end. They range in thickness from one-half to 1 cm. Thin, yellowish-brown, ovate, concave, irregularly margined scales adhere to the rhizome and stipes. The rhizome is green in color internally as are the official Aspidiums.

Microscopic—D. oregana differs from the official Aspidiums as follows: Many of the epidermal cells give off scales composed of elongated thin-walled cells with slightly irregular or toothed marginal cells. Glandular hairs are present on the margins of the scales and possess unicellular glands, unicellular or multicellular stalks, and are simple, non-branched and uniseriate. The glandular head is globose to orbicular in shape and measures up to 73 microns in diameter. The ovate scales usually possess two unicellular stalked glands at the base and a multicellular, uniseriately stalked gland at the tip. The multicellular stalks possess up to five cells (Fig. 3). The stem bundles are four to six in number. Glandular trichomes are absent in the intercellular air spaces of the cortex and pith. Two xylocentric vascular bundles are embedded in the parenchyma forming the central matrix of the stipe.

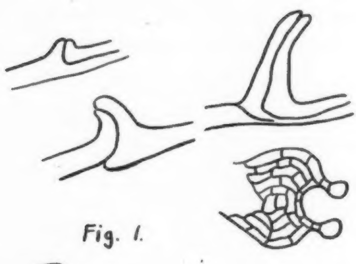


Fig. 1.

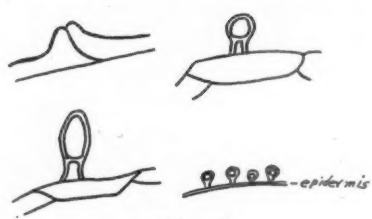


Fig. 2.

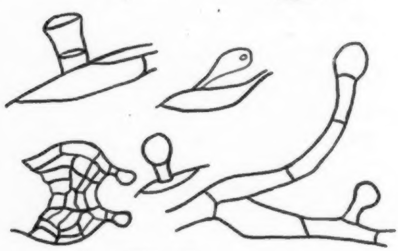


Fig. 3.

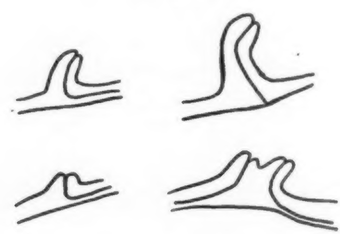


Fig. 4.

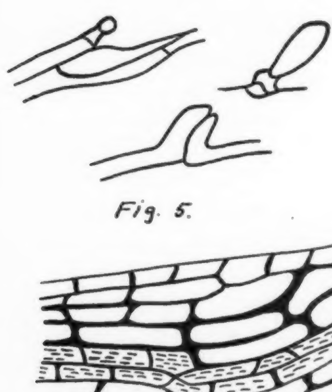
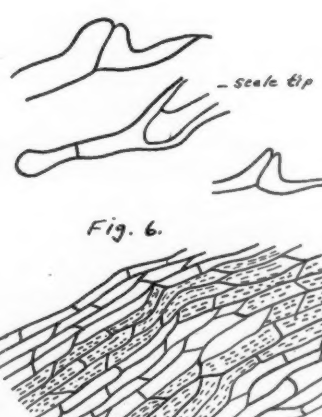


Fig. 5.



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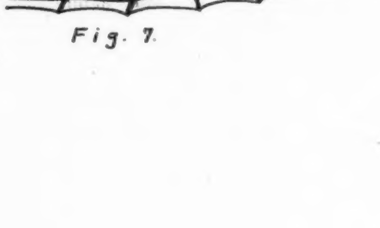

Fig. 7.

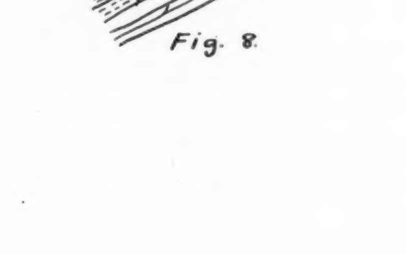

Fig. 8.

V. *Polystichum andersoni* Hopkins.

Macroscopic—The rhizomes are stout and occur either erect or decumbent in the soil. They are cylindrical and nearly straight in shape, or curved and tapering toward one end. They range in thickness from one-half to 1 cm. and are covered with the imbricate stipe bases of old fronds, especially in the apical portions. Thin, pale yellowish-brown, large, linear to ovate, denticulately margined scales adhere to the rhizome and stipes. The rhizome is green in color internally as are the official Aspidiums.

Microscopic—*P. andersoni* differs from the official Aspidiums as follows: Many of the epidermal cells give off scales having elongated, thin-walled cells with many of the marginal cells prolonged into fine hair-like projections, each projection consisting of two parallel and contiguous cells (Fig. 4). Glands are absent. The stem bundles are four to six in number. Glandular trichomes are absent in the intercellular air spaces of the cortex and pith. Four to five xylocentric bundles are imbedded in the parenchyma forming the central matrix of the stipe.

VI. *Woodwardia radicans* (L) Swartz.

Macroscopic—The rhizomes are woody and stout and occur obliquely in the soil. They are cylindrical and nearly straight in shape, or curved and tapering toward one end. They range in thickness from one-half to 1 cm. and are covered with the imbricate stipe

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DESCRIPTION OF PLATE (Ramenta or Scales).

FIG. 1—*Dryopteris Filix-mas* (L) Schott.

FIG. 2—*Dryopteris arguta* (Kaulfuss) Watson.

FIG. 3—*Dryopteris oregana* C. Christensen.

FIG. 4—*Polystichum andersoni* Hopkins.

FIG. 5—*Wodwardia radicans* (L) Swartz.

FIG. 6—*Athyrium alpestre* var. *americanum* (Butters).

FIG. 7—*Asplenium trichomanes* L.; stippled portion represents reddish-brown stripes.

FIG. 8—*Cryptogramma acrostichoides* R. Brown; stippled portion represents reddish-brown stripes.

bases of old fronds. Thin, bright yellowish-brown, large lanceolate-attenuate scales adhere to the rhizome and stipes. The rhizome is green in color internally as are the official Aspidiums.

Microscopic—*W. radicans* differs from the official Aspidiums as follows: Many of the epidermal cells give off scales having elongated thin-walled cells, with the marginal cells prolonged at intervals into fine, hair-like projections, each projection consisting of two parallel and contiguous walls. Occasional small, globose to oblong, sessile or non-sessile (short-stalked) glands are found on the margins of the scales (Fig. 5). Glandular trichomes are absent in the intercellular air spaces of the cortex and pith. The mature stem portions are monocyclic and the protoxylem of the xylem is mesarch. The stem bundles are two to four in number. In the stipe the cell wall between the endodermis and the inner cortex is excessively thickened, or about nine to ten microns in thickness. Two to four xylocentric vascular bundles are imbedded in the parenchyma forming the central matrix of the stipe.

VII. *Athyrium alpestre* var. *americanum* Butters.

Macroscopic—The rhizomes occur erect or decumbent in the soil with many branches and in large rounded tufts. They are cylindrical and nearly straight in shape, or curved and tapering at one end. They range in thickness from one-quarter to one-half cm. Many thin, ovate-attenuate, light to dark brown scales adhere to the rhizome and stipes. The rhizome is green in color internally as are the official Aspidiums.

Microscopic—Many of the epidermal cells give off scales having elongated thin-walled cells with the marginal cells prolonged at intervals into fine hair-like projections, each projection consisting of two parallel and contiguous cells. No glands are present upon the scales except a globose, usually collapsed gland, up to 75 microns in diameter found at the tip of the scale (Fig. 6). The hypodermis is discontinuous in cross-section and a crescent to gutter-shaped meristele is usually present as one of the rhizome bundles. The mature stem portions are monocyclic and the protoxylem of the

xylem is mesarch. The stem bundles are two to five in number. Two xylocentric vascular bundles are imbedded in the parenchyma forming the central matrix of the stipe.

VIII. *Asplenium trichomanes* L.

Macroscopic—The rhizomes occur erect or decumbent in the soil and are cylindrical and nearly straight in shape, or curved and tapering toward one end. They range in thickness from 5 to 10 mm. and are 1 to 3 cm. long. Numerous thick, linear-attenuate, latticed scales adhere to the rhizome and stipes. The rhizome is green in color internally as are the official Aspidiums.

Microscopic—*A. trichomanes* differs from the official Aspidiums as follows: Many of the epidermal cells give off scales having elongated cells with thick, reddish-brown walls. These scales may also be described as latticed. An unusually large, single, reddish-brown stripe may frequently be found coursing down the middle of the scale. The margins of the scales are entire and no glands are present (Fig. 7). Glandular trichomes are absent in the intercellular air spaces of the cortex and pith. One or more crescent-shaped meristeles are present as constituents of the rhizome bundles. Xylem parenchyma occurs only occasionally interspersed among the tracheids of the xylem. The stem bundles are two to five in number. A gutter-shaped xylocentric vascular bundle is imbedded in the parenchyma forming the central matrix of the stipe.

IX. *Cryptogramma acrostichoides* R. Brown.

Macroscopic—The rhizomes occur erect or decumbent in the soil and are short. They are cylindrical and nearly straight in shape, or curved and tapering toward one end. They range in thickness from 2 to 5 mm. Numerous thin, lanceolate-ovate, attenuate scales adhere to the rhizome and stipes. The rhizome is green in color internally as are the official Aspidiums.

Microscopic—*C. acrostichoides* differs from the official Aspidiums as follows: Many of the cells of the epidermis give off scales having elongated, thin-walled cells, pale yellow in color, and with occasional reddish-brown stripes. The margins are smooth and no glands are present (Fig. 8). Glandular trichomes are absent in the intercellular

air spaces of the cortex and pith. The stem bundles are four to six in number. The protoxylem of the xylem is mesarch. A xylocentric vascular bundle is imbedded in the parenchyma forming the central matrix of the stipe.

Summary

A histological comparison of the rhizomes and stipes of *Dryopteris Filix-mas* (L) Schott with those of certain other members of the Polypodiaceae family has been made. This study has established type descriptions and illustrations of the external and histological elements by which the plants may be identified.

Differences in the histological comparisons of each species were found to be few in number and have been described. Internal glandular trichomes were found to be absent in all but *D. arguta*. The starch grains were found to be of no value in the identification of a species.

The presence of characteristic ramenta or scales in all species was found to be of use in identifying a species. Definite similarities in histological structure prevail and further render the separation of each species from another, upon the basis of its microscopical description, difficult.

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CONSTITUENTS IN RED BLOOD CELLS OF VALUE IN WOUND HEALING

By Saul Caspe

MOORHEAD and Unger (1) in a recent report demonstrate that in a few cases the discarded red cells, a by-product of the present plasma program, accelerated the healing of wounds. Their report also indicates 100 ml. of red cells contain 35 grams of protein, but the possible role of constituent proteins is not mentioned. This study has received considerable publicity and a newspaper editorial predicted that the active organic substance will be discovered.

It is a little premature to expect the biochemist to isolate the active substance without first ascertaining whether the healing virtue of these red cells is definitely established. The biologist must then determine the mechanism or manner in which the healing occurs. Preliminary reports emanating from the Mayo Clinic tend to establish the celerity in healing (non-healing) wounds by dusting red blood cell powder upon their exposed surfaces. The results of this study confirm the initial clinical success of Moorhead and Unger.

Is the application of red cells in this connection accidental, intuitive or based on the accumulated knowledge of the properties of their constituent proteins and amino acids? There is neither indication in these studies of the manner in which the healing is promoted nor the substances responsible for this phenomenon. It is of immediate interest to analyze from this latter standpoint the substances contained in red cells that may be responsible for its wound healing properties.

In the manufacture of blood plasma the red cells are packed into approximately one-half of their previous volume in whole blood, and it is reasonable to expect that certain cell constituents will be found in red cells in greater concentration than in whole blood. In fact there is ample evidence to show that this actually occurs. What are the constituents in blood that are known to be accelerators in the healing process? They are glutathione, hemoglobin, creatine (2), and allantoin.

Baker (3 and 4) has demonstrated that glutathione and hemoglobin will stimulate the growth of various tissues *in vitro*. The importance of these substances in cell respiration has been indicated. Hammett (5) reported in 1929 the cell proliferation response to the sulfhydryl group. By use of thioglucose he healed artificially induced wounds in rats. He was an advocate of the importance of glutathione in developmental growth and demonstrated its values *in vitro* upon plant and animal tissue. Glutathione is a tripeptide, glutamyl-cysteinyl-glycine, and contains the sulfhydryl group. He (6) explained in a later report that the cysteine accelerates cell proliferation; the glycine accelerates protein reconstitution, the glutamic acid accelerates differentiation and consequent organization. Bowman (7) showed that there is 27.5 mg. per cent of glutathione in whole blood and 69.5 mg. per cent of glutathione in red cells. Anderson (8) has shown that there are 14.96 grams of hemoglobin in 100 cc. of human male blood.

Recently Caspe (2) indicated that creatine stimulates the growth of various tissues *in vitro* and that it has clinical value in the healing of wounds. Chemical analysis of the discarded red cells indicates that they contain glutathione, hemoglobin and creatine in active concentrations.

Macalister (9) and Robinson (10) have reported the value of allantoin as a cell proliferant in the healing of wounds. Beard and Pizzolato (11) injected 6-12 mg. of allantoin in animals and observed an average increase of 43-58 per cent in muscle creatine. This fact may account for some if not all of the healing activity of allantoin. Anderson (8) found that bovine blood contains 10-15 mg. per cent of allantoin.

Summary

Red cells, a by-product of the plasma program, contain glutathione, hemoglobin, creatine and allantoin.

These organic constituents have previously been applied to wound healing.

A possible mechanism for the action of allantoin is suggested to us by the work of Beard *et al* who found that allantoin has an effect upon creatine metabolism.

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SCIENTIFIC RESEARCH CAN BE PLANNED WITHOUT REGIMENTING SCIENTISTS

By T. Swann Harding

ACCORDING to the classic doctrine of unplanned scientific research science is divided into two parts. Part 1 is practical research or technology, and the scientist who works at it has for his primary objective the solution of a specific problem. He is essentially a technologist and his work can be planned advantageously. But he is a scientist of the lower order.

Part 2 is "pure" research. The scientist who works at it is an ethereal, sensitive being of the higher order, akin to a musician or an artist. Unlike practical research, "pure" research cannot be planned. It can only achieve results if wholly unplanned and adventitious.

Of course, technology is important, but it is not the real thing. It is also a rather worldly pursuit. The pure scientist must remain wholly unconcerned with economics, politics, and such other sordid matters, in order to maintain his dispassionate objectivity.

That habit of his naturally leads to uncontrolled applications of his objective scientific findings, and that is too bad. But the planning of scientific investigation is not the remedy. For the pure scientist cannot see to the end of his investigations. He works by hunch and by chance. He must have faith and follow where the truth leads.

He cannot work by a time-table, and all planning of his activities is fatal. He cannot even be judged by his results, or the poundage of his publications, though he actually is judged by the latter, and his advancement often hinges thereupon. His great moments of insight and inspiration often occur when he is off duty.

Most of his brilliant successes are the result of pure chance. He must lack supervision at all times. He must be perfectly free to do as he pleases, take advantage of his accidents, and direct his work for himself. That is the doctrine, and it is so fallacious as to be pernicious.

Recently many American scientists have become exercised for fear a bill authorizing scientific and technical mobilization of Ameri-

can scientists and science might be passed by our Congress. The chemists and engineers especially assert that this would lead to regimentation and disaster.

One lachrymous scientist, for instance, lugubriously wrote our leading scientific news weekly in protest and abject fear. If the Kilgore Bill (S. 702 78th Congress, First Session) for scientific and technical mobilization actually passed, he declared that freedom of thought, private enterprise, and the spirt of free inquiry would be destroyed, while governmental dictatorship and regimentation would take over. He dubbed the proposal "A Bill for the Regimentation of Science."

He displayed great fear of a governmental administrator with a board of scientific advisers to coordinate scientific research so as to get the best out of it. Such procedure would have squelched Galileo, Darwin, Morton and Warren, and the Wright brothers at the start, because governments are always reluctant to finance experimentation along new lines or to accept the new—quite as our private industry always has been, if you look into its history.

This melancholy scientist continued that the progress of science into new and unforeseen fields would end with passage of such a law, because only private capital and foresight had ever made this possible —a statement in clear conflict with the history of scientific development. Individual initiative could no longer be exercised. For no political agency could possibly have the perspective properly to evaluate scientific initiative and enterprise, except in terms of existing categories. The next step in this terrible program of complete "socialization" would be the regimentation of religon.

This ghastly exhibit reveals the almost incredible ignorance of scientists when they attempt to consider matters outside their own narrow field. That ignorance is quite natural, as it has so long been a deliberate objective of "pure" scientists to avoid worldly matters. That research may be performed quite as freely and successfully under government as under private subsidy and direction is a matter of established fact to the present writer, who was for fourteen years engaged in research in Federal Government laboratories and for four years in private industry.

But the vast majority of research, like his own, is quite ordinary in character. It deals with the establishment of detailed facts. Genius is rare indeed, and markedly different from scholastic brilliance or

extraordinary technical skill. It is ill-understood in its own time, not addicted to working on straight salary, unpredictable, and bound to follow its own route to achievement, regardless of subsidies, plans, or supervisors.

Ordinary research can very definitely be coordinated and organized. It is better so. It does not seek great unknown truths, but subordinate, substantiating facts. Organized research can enrich knowledge a great deal better if well planned and organized. It cannot be expected to enrich vision, as that is the function of genius.

The idea that the research worker is inhibited in government service is false. A research worker has far more difficulty in attaining freedom to pursue truth in private industry than he does in government. There all sorts of tabus and prohibitions surround him. Industrial secrecy pursues him, and the office politics that appears to afflict every concern in private enterprise dogs his steps. He is much more likely to attain freedom in a government than in a private laboratory.

A nation can win a total war only by the full and efficient utilization of its scientific knowledge. Unfortunately it is not so clear, though quite as true, that the nation which wins at peace is also the one that makes the fullest, most efficient planned use of its scientists and its scientific knowledge.

To adopt the view that the common run of scientists are divided into prima donnas devoted to "pure" research and hewers of wood and drawers of water who engage in impure research is wholly wrong. To believe that the best scientists, genius excepted, make their most notable contributions to human knowledge fortuitously is highly inaccurate.

In modern successful research scientists work in teams. They proceed within the plane of reference of existing scientific knowledge. No astronomers base their efforts upon ancient astrology, nor do modern chemists work in accord with the tenets of ancient alchemy. It is not a case of starting in anywhere and doing what whim dictates. Scientific research workers are primarily regimented by the current character of what science regards as true.

Frequently, it is true, an individual manages to procure for himself the requisite degrees, topped by a doctor of philosophy, and a job in a research laboratory, without there having been much planning in advance. Such individuals often regard it as their right to pick

out any problem that appeals to them, and to continue hacking at it in their own way for years on end, without regard to its importance or the probabilities against their solving it.

"Pure" research laboratories are cluttered with such individuals during peacetime. They are relatively untouchable. It is considered indecent to expect them to conduct themselves logically and scientifically in the pursuit of their daily work. The assumption is that, if they have proper equipment and material, the miracle will take place and additions to knowledge will result inevitably.

This simply is not true. Only outstanding genius should be afforded the luxury of such treatment. The common run of pure research workers are not a cut above the technologists but, because they have the privilege, they often start more problems than they can attend or hope to finish, clutter their minds, notebooks, and laboratories with trivia, waste time and money, and come out exactly nowhere.

The modern professional man arose out of mystery. He is descended from primitive priestcraft. As magician, alchemist, and astrologer he dealt with the unknown, became sacrosanct, withdrew into himself, and resented the intrusion of mere laymen. He financed himself and felt that what he did was nobody's business but his own. Curiously enough he has retained these tendencies even when graduated from modern schools of law, medicine, or science.

Physicians have long masked their ignorance and incompetence by a refusal to accept proper supervision. They have long tended to be aloof from laymen, to treat them as a subordinate form of human beings who could not be expected to understand the great mysteries which are open books to doctors. This physicians have frequently managed to do, while writing a Latin prescription for the equivalent of a popular patent medicine, regarding the ultimate physiological properties of which they are broadly ignorant.

So, the worker in "pure" research has managed to fence himself off even from his fellows who work in lowly technology. He feels himself superior, not only to laymen, but to more practical workers in the same field. Meanwhile the technologist, or practical research worker, insofar as he works in industry, shares the viewpoints of monopolistic private enterprise and fears any organization of science on a national basis as inimical to business.

Frequently, however, the pure scientist's aloofness is a screen for his ignorance or incompetence, just as his loudly proclaimed objectivity and dispassion too often become screens for his lazy refusal to study and comprehend the nature of the society in which he lives. Behind these screens he can be and often is doing the most trivial things in a most disorderly way.

Without intelligent direction and supervision, workers in pure research, as those who really know their habits well can attest, are very much inclined to be extraordinarily inefficient. They take too much pains in cases where few are required. They read, abstract, maul, and thieve from the existing literature incontinently. They follow the latest fads and seek shrewdly to attach their own minor activities to the notable discovery or finding of some really outstanding worker.

The minute someone says: "All this equipment and all these workers should have some broad objective, some general guidance, direction, and supervision. They should advise and counsel one another. They should proceed in accordance with general plans, subject to plenty of variation in detail, drawn up by leaders in this field of scientific endeavor."—the minute this is said, they cry: "Regimentation!"

They really are very much frightened, too. They are afraid that experts might investigate and find out how trivial their activities are and how cluttered their notebooks, laboratories, and minds. They would much prefer this did not happen. Yet just that should occur.

It is true that each fundamental discovery does have repercussions throughout the realm of science, but each rests on the work of many, not wholly upon a stroke of genius on the part of an individual. In the long run new discoveries proceed from fundamental research conceived in intellectual terms. But all research should have definite plan and purpose.

It would be a good thing for "pure" scientists to sit down from time to time and try to calculate out the returns the public gets from them by honestly estimating their salary and expenses. Many such workers, lacking organizing ability and a sense of order, spread their efforts thinly over many fields and subjects, dissipate their energies, and never produce anything meriting publication.

Research should be rigidly planned from beginning to end. Changes in course have to be made as need be, quite as in practical research, but the frame of reference should remain intact. The research worker often displays the confusion in his mind by the confusion in the reports he prepares. If he cannot think clearly, correctly, logically, and in orderly fashion, he can neither work nor report thus.

Lavish publication with failure to digest results and to coordinate work with other work is common. Many signal discoveries long lie dormant because bibliographical work is neglected. Relatively few even know how to run down references, especially if these prove a bit difficult. Such bibliographic work and study lacks due recognition in the field of pure science.

Pure science needs more workers to abstract, digest, collate, and evaluate available information. The interpretation, coordination, and accurate presentation of pure science in direct language is urgent. Darwin is said to have accomplished as much by putting together scattered bits of information derived from others as by his own personal investigations.

Scientific research requires a general staff of its own, just as an army or navy does. Some problems are at dead-end streets for lack of knowledge or instruments not yet in existence. Some problems, though attractively technical and difficult, are neither pressing nor important at this stage of progress. In some instances methods and equipment should really be tested out with care before an effort is made to proceed. In others the literature merits diligent search before anything is done in the laboratory.

There is need, then, for some centralized planning agency to act as a general staff for scientific research. It need not be rigidly governmental. As a matter of fact it should have on it both governmental and private-industry scientists, both technologists and workers in pure research, and also statesmenlike, foresighted individuals who are not scientists at all.

In every modern nation the national academy or institute of science, whichever you choose to call it, should be the core and the key of organized society. It should have as its members not only physical and biological, but also social scientists. It should examine into the needs of the society, formulate problems to be solved, and make efforts

to have them solved with the least possible duplication, confusion, waste, or inefficiency.

Scientific men have neglected to act scientifically in their own work and with regard to applications made of the knowledge they create. We need some organized body to stimulate activity here, to decide which scientists are best fitted and which laboratories best equipped to undertake specific investigations, and to see to it that all our scientific talent and resources are utilized fully and efficiently at all times, in peace or at war.

Nothing, least of all science, can be managed well by chance and by whim, and hope to get anywhere. There must be planned, coordinated activity, which offers intelligent supervision, direction, and guidance without interference with the spirit of free inquiry. Such guidance can be planned and it does no harm to science to plan it.

Scientists can still make discoveries by accident or follow unexpected paths to truth as these open up. Genius can still flower as it always has in spite of obstacles—or because of them. The assumption that every petty, little Ph. D. in "pure" research is a genius is too ludicrous to consider seriously.

Finally, we require in peacetime as well as when at war a mechanism for the proper economic and social utilization of scientific knowledge. In the long run the public pays for all research investigation. It, therefore, should benefit therefrom. The public welfare, not profits; service, not exploitation, should be paramount.

Our refusal to make scientific use of scientific knowledge has brought our civilization to the brink of disaster. That disaster can be avoided only if we elect to reverse our attitude towards science and use it consistently for the upbuilding of the good society.

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American Journal of Pharmacy

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